REMARKS

Claims 1-85 are pending. Claims 3, 5, 10-15, and 26-85 have been withdrawn from consideration as directed to non-elected inventions. Claims 1, 2, 4, 6-9, and 16-25 are rejected. Claims 18-21 have been amended. Claims 43-84 have been canceled. Claim 86 has been added. Rejoinder of Claims 3, 5, 10-15, 26-42, and 85 is requested. Reconsideration and allowance of Claims 1-42, 85, and 86 in view of the above amendments and the following remarks is respectfully requested.

The Rejection Claims 1, 2, 4, 6-9, and 16-25 Under 35 U.S.C. § 102(b)

Claims 1, 2, 4, 6-9, and 16-25 have been rejected under 35 U.S.C. § 102(b) as being anticipated by WO 97/18790, issued to Pascual et al., in light of Spevak et al., *J. Med. Chem. 39*:1018-1020, 1996. Withdrawal of the rejection is requested for the following reasons.

The Pascual reference relates to therapeutic peptides, vaccines, and diagnostic agents for the treatment of pathogenic infections. The reference discloses therapeutic peptides, vaccines, and diagnostic agents comprising an attachment molecule that mimics the adhesion molecule of a pathogen and binds with receptor molecules on a cell selected from the group consisting of leukocytes, endothelial cells, epithelial cells, and other target cells of the host.

The Spevak reference discloses synthetic carbohydrates in an acidic multivalent assembly as nanomolar P-selectin inhibitors. The high-affinity P-selectin inhibitors are prepared from polymerized glycoliposomes with an acidic matrix lipid. The inhibitors are capable of preventing binding between the adhesion molecule and its corresponding ligand.

The Examiner is of the opinion that the combined teachings of the Pascual reference and the Spevak reference describe the claimed invention. According to the Examiner, the Pascual reference discloses molecules that are adhesins binding to ligands on the surfaces of cell membranes and the Pascual reference discloses competitive inhibitors of known adhesin/ligand

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

binding strength under shear forces, which meet the definition provided in the claimed invention. The Examiner concludes that the method of the Pascual reference in light of the Spevak reference anticipates the claimed invention. In addition, the Examiner is of the opinion that the Pascual reference inherently anticipates the claimed invention. Applicants respectfully disagree.

Claim 1 recites a method for changing binding strength of an I-FABSDAM to a FABSDB-L for the I-FABSDAM. The method includes the steps of (a) binding the I-FABSDAM with the FAMSDB-L and (b) changing a bond stress on the I-FABSDAM, wherein the binding strength between the I-FABSDAM and the FABSDB-L increases when the bond stress increases and decreases when the bond stress decreases. Claims 2, 4, 6-9, 16-25 depend from Claim 1.

Neither the Pascual reference nor the Spevak reference describes every element of Claim 1. The Spevak reference discloses the synthesis of carbohydrates that bind to P-selectin. Glycoliposomes containing the carbohydrates were assayed for inhibition of P-selectin IgG chimera binding to HL-60 cells. As noted by the Examiner, the Pascual reference discloses attachment molecules, such as adhesions, that bind to ligands on the surfaces of cell membranes. The reference discloses binding vaccines, peptides, or diagnostic agents with the target cells through the binding ability between the attachment molecules and their ligands/receptors on the target cells. Therefore, both references arguably disclose step (a) of the claimed method. However, the teachings of both references end at the binding of an attachment molecule with the ligand/receptor. In the Spevak reference, once the P-selectins on HL-60 cell are occupied by the carbohydrates, inhibition of P-selectin IgG chimera binding to the cells is achieved. In the Pascual reference, once the therapeutic peptide, vaccine, or diagnostic agent binds to the target cell, therapeutic or diagnostic purpose has been accomplished. Neither reference discloses nor suggests step (b) of the claimed invention, i.e., after the binding, changing a bond stress on the

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1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

I-FABSDAM, wherein the binding strength between the I-FABSDAM and the FABSDB-L increases when the bond stress increases and decreases when the bond stress decreases. In addition, because both references have achieved their purposes by merely accomplishing step (a), neither reference provides an apparent reason or any motivation to add step (b).

Because the cited references fail to exactly describe the claimed invention, the references are not anticipatory. Withdrawal of the rejection is respectfully requested.

Furthermore, applicants submit that the cited references fail to teach, suggest, provide motivation or reason to combine, or otherwise render obvious the claimed invention.

The Rejection of Claims 1, 2, 4, 6-9, and 16-25 Under 35 U.S.C. § 102(e)

Claims 1, 2, 4, 6-9, and 16-25 have been rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent Application Publication No. 2004/0247611, issued to Bargatze et al. Withdrawal of the rejection is requested for the following reasons.

The Bargatze reference discloses assays for identifying pathogen-ligand interactions under shear conditions. The assays disclosed in the reference use an interaction between the pathogen adhesion molecule and its corresponding ligand to identify pathogens.

It is the position of the Examiner that the terms I-FABSDAM and FABSDB-L are defined in the specification to represent a genus of molecules with adhesion activity and adhesion binding activity, respectively. According to the Examiner, the Bargatze reference anticipates the claimed invention. Applicants respectfully disagree.

The Bargatze reference fails to describe every element of the claimed invention. The Bargatze reference fails to disclose an isolated force-activated bond stress-dependent adhesion molecule (I-FABSDAM), as recited in the claimed invention. The term, "I-FABSDAM" is defined at page 24, lines 18-20 of the specification: I-FABSDAM refers to FABSDAMs that are not in the same context in which they exist in nature, including their natural *in vivo* context. In

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CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

contrast, the Bargatze reference discloses pathogen-ligand adhesive interaction. The ligand or target cells expressing the ligand can be immobilized on a substrate. However, the adhesion molecule is immobilized on the pathogen to be identified. Therefore, in contrast to the claimed invention in which the adhesion molecule is an isolated adhesion molecule, the adhesion molecule described in the Bargatze reference is in its natural state.

In addition, similar to the Pascual and Spevak references discussed above, the Bargatze reference only teaches step (a) of the claimed method, i.e., the binding between an adhesive molecule on a pathogen and its ligand on a substrate. There is no teaching of step (b) in the Bargatze reference, i.e. after the binding, changing a bond stress on the adhesion molecule, wherein the binding strength between the adhesion molecule and its ligand increases when the bond stress increases and decreases when the bond stress decreases.

Because the cited reference fails to exactly describe the claimed invention, the reference is not anticipatory. Withdrawal of the rejection is respectfully requested.

Furthermore, applicants submit that the Bargatze reference fails to teach, suggest, provide an apparent reason or any motivation to add step (b) to arrive at the claimed invention.

The Rejection of Claims 1, 2, 4, 6, and 7 Under 35 U.S.C. § 102(b)

Claims 1, 2, 4, 6, and 7 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Brooks et al., *Annals of the New York Academy of Sciences 416*:319-331, January 1983. Withdrawal of the rejection is requested for the following reasons.

The Brooks reference describes the attachment mechanism employed by pathogens. Specifically, the reference discloses interactions of erythrocytes with bacteria under shear stress.

According to the Examiner, the Brooks reference discloses isolated Aeromonas salmonicida strain 438, which comprises the adhesion molecule, and contacting the isolated adhesion molecule with its ligand attached to a particle, specifically an erythrocyte under shear

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1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

stress. The Examiner concludes that the Brooks reference anticipates the claimed invention. Applicants respectfully disagree.

The Brooks reference fails to describe every element of the claimed invention. The Brooks reference fails to disclose an isolated force-activated bond stress-dependent adhesion molecule (I-FABSDAM), as in the claimed invention. We believe that the Examiner's conclusion may be based on misreading of the present application. On page 24, lines 17-19, the specification states that "I-FABSDAMs" refer to FABSDAMs that are not in the same context in which they exist in nature, including their natural *in vivo* context. Therefore, the claimed invention recites an adhesion molecule that is not in its natural state. The Brooks reference discusses the interactions of erythrocytes with bacteria under shear stress. In contrast to the claimed invention, the adhesion molecules and their ligands disclosed in the Brooks reference are both in their natural states.

Because the Brooks reference fails to exactly describe the invention, the reference is not anticipatory. Withdrawal of the rejection is respectfully requested.

Furthermore, applicants submit that the Brooks reference fails to teach, suggest, provide an apparent reason or any motivation to make, or otherwise render obvious the claimed invention.

Claims 18-21

Claims 18-21 have been amended for the purpose of clarity.

As amended, Claim 18 recites a method of Claim 1 in which the I-FABSDAM is attached to a particle or a surface. The particle is selected from the group consisting of bacterial pili, organelles, prokaryotic cells to which said I-FABSDAM is not native, eukaryotic cells to which said I-FABSDAM is not native, viruses, organisms, nanoparticles, microbeads, and microparticles. The surface is selected from the group consisting of cell membranes, device

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1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

surfaces, and synthetic substrate surfaces. Claim 19 depends from Claim 18. Claim 19 further requires that the FABSDB-L is attached to the particle or the surface.

As amended, Claim 20 recites a method of Claim 1, in which the FABSDB-L is attached to a particle or a surface. The particle is selected from the group consisting of bacterial pili, organelles, prokaryotic cells to which said I-FABSDAM is not native, eukaryotic cells to which said I-FABSDAM is not native, viruses, organisms, nanoparticles, microbeads, and microparticles. The surface is selected from the group consisting of cell membranes, device surfaces, and synthetic substrate surfaces. Claim 21 depends from Claim 20. Claim 21 further requires that I-FABSDAM is attached to the particle or the surface.

Therefore, Claims 18-21 are directed to methods for changing binding strength of an I-FABSDAM to a FABSDB-L according to the claimed invention, in which one of the I-FABSDAM and the FABSDB-L, or both, are immobilized on a particle or a surface. Because none of the cited references disclose a method including both steps (a) and (b) of the claimed invention, in which one of the I-FABSDAM and the FABSDB-L, or both, are immobilized on a particle or a surface, Claims 18-21 are novel. In addition, because the cited references fail to teach, suggest, provide any motivation to make, or render obvious the methods of Claims 18-21, Claims 18-21 are nonobvious.

New Claim 86

New Claim 86 has been added. Claim 86 depends from Claim 1. Claim 86 recites the combination of the elected species previously indicated as allowable by the Examiner. Specifically, Claim 86 is directed to the method of Claim 1 and recites, in pertinent part:

the I-FABSDAM comprises a FimH polypeptide or the lectin domain of FimH polypeptide and is attached to a first pili carrier particle;

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CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

the FABSDB-L comprises a mannose and is attached to a second pili carrier particle; and

the bond stress is increased resulting in the increased binding strength between the I-FABSDAM and the FABSDB-L.

Support for the amendment can be found throughout the application as originally filed. See, for example, page 13, lines 15-30 and page 21, lines 14-28.

Rejoinder of Claims 3, 5, 10-15, 26-42, and 85

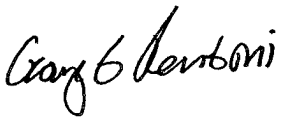
Applicants have elected the invention of Group I, Claims 1-42 and 85, for examination. Because the claims directed to the elected species, Claims 1, 2, 4, 6-9, and 16-25 are patentable over the cited references, rejoinder and allowance of Claims 3, 5, 10-15, 26-42, and 85, directed to non-elected species, is requested.

CONCLUSION

Applicants believe that Claims 1-42, 85, and 86 are in condition for allowance. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicants' attorney at 206.695.1755.

Respectfully submitted,

CHRISTENSEN O'CONNOR
JOHNSON KINDNESS[PLLC]



George E. Renzoni, Ph.D.
Registration No. 37,919
Direct Dial No. 206.695.1755

GER:CFW/md

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS[PLLC]
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206 682.8100